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REVIEW

A Review of the Ethical and Legal Challenges in Clinical Trials

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Abstract: Clinical research is the cornerstone of the progress recorded in psychiatry in the last six decades, or of what is called the psychopharmacological revolution. Regardless of the stage of clinical research, there are sensitive ethical and legal aspects that may appear during this process, and such challenges have to be acknowledged in order to preserve its scientific value, integrity, and centered-on-the-patient-wellbeing core principles. Also, adequate strategies focused on preventing the risk of ethical misconduct and litigation have to be found to avoid a loss of trust in the results of clinical research, to protect vulnerable populations from abuse, and to ensure a legally stable environment for investigators. In order to explore these practical problems, a narrative review was performed through a search in PubMed and Google Scholar databases. The main ethical risks detected in clinical research were related to errors in the methodology of obtaining informed consent, monitoring the participant's safety during the clinical trial, and falsifying collected data. Several famous cases of ethical misconduct were found and analyzed, and methods to decrease the risk of the re-appearance of such problems have been listed. In conclusion, this review is an invitation to explore the complexity of the methodology of clinical research and its ethical and legal risks, as well as to find new ways to mitigate the possibility of such risks related to the research process.

Keywords: clinical trial; volunteers; informed consent; vulnerable population; pharmacological agents; psychopharmacology; ethical misconduct

INTRODUCTION

Clinical research is an essential component of the broader paradigm of evidence-based medicine that is focused on ensuring scientific progress in healthcare. Although the evolution of medicine is an important objective, it must always be kept in mind when discussing clinical trials that the ultimate goal is to increase the quality of services offered to patients and improve their prognosis and chances of regaining a normal life. To refer only to the field of psychiatry, the developments recorded in the armamentarium of psychotropics in the last six decades represent a veritable revolution that allowed a change in the nosological paradigm of psychiatric disorders. Due to this change, which showed there is a biological basis for mental illnesses and that pharmacological agents can mitigate their symptoms, the stigmatization and the tendency to institutionalize patients with such diagnoses decreased and are expected to diminish further in the near future.

The importance of clinical research is illustrated by the high number of trials identified by a search in the International Clinical Trials Registry Platform (ICTRP), a World Health Organization database, that reported the existence of 10606 depression studies in 2024 [1]. According to the US National Library of Medicine database for clinical trials (ClinicalTrials.gov), more than 530000 studies are registered, out of which over 200000 are exploring a drug or a biological product, regardless of the pathology targeted, at the beginning of 2025 [2].

The need to conduct clinical trials in psychiatry is supported by a large number of practical difficulties when confronting the reality of mental health problems. One of the most critical challenges for clinicians is to increase the rate of responsiveness in treatment-resistant psychiatric illnesses, being known that 30-35% of depressive disorders, 30% of schizophrenia spectrum disorders, and up to 25% of bipolar disorders do not respond well enough to the usually administered pharmacological agents [3-7]. Another significant motive to foster clinical research in the field of psychiatry is the continuous quest to find new formulae to enhance therapeutic adherence (e.g., other ways of administration for a particular substance, coupling

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the active drug with a vehicle that allows a slower release of the active substance so that the interval between administration could increase, or to find molecules with superior tolerability). Changes in the pharmacodynamic or pharmacokinetic properties of certain drugs that are already available for clinical use could lead to the discovery of new drugs with potentially superior properties. Covering emerging health needs, including mental health-related problems, such as the long COVID-19 syndrome, new psychoactive substances (NPS) use disorders, etc., is another important reason for conducting clinical trials.

Some of the above-mentioned directions of research have been more productive than others, while high expectations are related to the objectives insufficiently accomplished, like detecting pathogenic rather than symptomatic treatments or improving the tolerability of already existent drugs for treatment-resistant cases. For example, when discussing the improvement of treatment adherence, the discovery of long-acting antipsychotics that allow patients with schizophrenia to receive only two injections each year (i.e., paliperidone palmitate with 6-month release) could be considered significant progress [8-10]. The production of active metabolites as independent drugs, a process starting with tricyclic antidepressants, like nortriptyline from amitriptyline, or desipramine from imipramine, and continuing with new-generation antidepressants and atypical antipsychotics, like desvenlafaxine from venlafaxine, or paliperidone from risperidone, allowed for improving and diversification of pharmacokinetic and pharmacodynamic properties of the parent drugs [11-15]. Another direction of research is improving the pharmacodynamic properties of a racemic mixture by extracting only the most potent enantiomer, as was the case of escitalopram, levomilnacipran, or eszopiclone [16-20]. Even one of the most sensitive topics in psychopharmacology, i.e., the pathogenic vs. symptomatic treatments, acknowledged significant progress in the last years by the Food and Drug Administration (FDA) approval of monoclonal antibodies that target beta-amyloid peptides, like aducanumab, donanemab or lecanemab [20-23].

The responsibility for conducting clinical trials belongs to medical professionals, primarily doctors, but also to other categories of healthcare personnel – registered nurses, clinical psychologists, etc., who follow specific training programs before engaging in any research activity. Completing these training programs provides professionals with a common background of knowledge and skills necessary for participation in pharmacological studies. Specific certifications, such as Good Clinical Practice (GCP)– ICH Guidelines E6 R2, or qualifications for scoring scales and inventories used to measure the severity of clinical symptoms, have the aim to protect participants in clinical studies, reduce the risks of malpractice for investigators, increase the validity of data obtained from the research, and decrease the inter-rater variability of clinical scale results [24-27].

The Declaration of Helsinki regarding human experimentation originated in 1964 in the World Medical Association (WMA) statement and has been constantly revised ever since, with the last revision in 2024 [28-30]. This declaration is an essential step in the history of conducting research with human subjects, as it stipulates the fundamental principles of this domain, for example, the unconditioned respect for individuals and their right to self-determination and making informed decisions regarding their own health, including aspects pertaining to participation in clinical studies [28,30]. The primary duty of the investigators is to the patient or volunteer included in clinical studies, and the participant's well-being takes precedence over the interests of science and society [28-30]. This declaration also stipulates that ethical aspects are primordial and laws and regulations are only second in importance [28-30].

Ethical and legal errors in pharmacological research have the potential to harm not only study participants but also the integrity of the entire research process, thus indirectly affecting a very large number of patients who could benefit from a specific investigational product once it is approved. This narrative review is dedicated to highlighting the most relevant domains of clinical research that are vulnerable to malpractice risk and to investigate possible ways to decrease the probability of its onset.

MATERIALS AND METHODS

Two electronic databases (PubMed and Google Scholar) were searched for the terms „malpractice," OR „ethical issues," OR „methodological errors," OR „legal issues," AND „clinical trials," OR „pharmacological research," OR „drug research," OR „psychopharmacology." All primary and secondary reports published in English were selected if they corresponded to the inclusion criteria and did not meet the exclusion criteria. In order to ensure adequate coverage of this topic, grey literature was also searched for papers published in English. The period chosen for published papers was between the inception of each database and January 2025. Inclusion criteria: all types of research and commentaries, press releases and related sources of information; all stages of clinical trials, if related to the field of psychiatry; pharmacological interventions, either alone or in combination with other interventions. Exclusion criteria: non-pharmacological interventions used alone; reports that did not contain precise data on ethical or legal issues related to clinical trials in psychiatry; undefined outcomes or imprecise source of the referenced studies.

RESULTS

From the clinical research perspective, ethical and legal error problems appear when a doctor participating in clinical trials (hereinafter referred to as "investigator") does not comply with the correct way of obtaining adequate informed consent, mismanages patient safety measures, or falsifies research data. These actions can lead to serious consequences for participants, undermine the validity of clinical trial results, and negatively impact the medical community and society as a whole through the decrease of individuals' chances of getting the optimal cure.

Ethical and legal challenges related to obtaining informed consent

Signing informed consent is the first procedure a participant in a clinical trial has to perform prior to any study-related procedures [31]. This step is mandatory in the era of clinical trials conducted under rigorous ethical principles, according to the principles of the

Declaration of Helsinki [28-30]. The procedure of informed signed consent is mentioned in the GCP guidelines and reflects the principles of absolute respect for patients' autonomy and their right to be informed in every aspect of the trial that is relevant to their own health [24-27]. Also, the Declaration of Helsinki stipulates that whenever the participants are unable to give their own consent, surrogate consent may be obtained from an individual acting in the participant's best interest, but the consent of the participant still needs to be obtained if at all possible [28-30,32]. The cases when this procedure is applicable are also presented in the Declaration of Helsinki [28]. The investigator must ensure that this consent is given freely, without any form of coercion, and with a comprehensive understanding of the implications of the study [28].

Possible errors in this domain, which are compatible with a risk of malpractice, are (a) a failure to disclose potential risks of the trial, (b) providing false or intentionally incomplete information, and (c) coercing patients to participate in the study.

For example, if an investigator conducting a study fails to properly explain to participants the adverse events or health risks of the investigational product, patients could be exposed to a danger to their health that they did not voluntarily assume in the very beginning. A study exploring the proportion of participants in clinical trials (N=135 cohorts) who were aware of the different elements of informed consent showed that only 52-75.8% understood what they were signing [33]. According to this study, 74% of the participants were aware of potential benefits and less than 70% of the study's aim, while 66% understood the rule of confidentiality [33]. Also, the proportion of participants who understood the informed consent did not increase during the 30 years of the studies included in the review [33]. These data indicate the need for better communication between investigators and participants during the signing of the informed consent form.

According to the GCP-ICH, both the informed consent discussion and the written informed consent form and any other written information to be provided to subjects should include explanations of the testing hypothesis process involved by the clinical trial, which is the purpose of the trial, understanding the fact that the treatment is not validated and what is the probability of random assignment to each treatment/placebo [24-27]. Also, the participant must receive adequate information about the study procedures to be followed, including all invasive procedures, which are his/her responsibilities, those aspects of the trial that are experimental, and the reasonable risks that can be anticipated or inconveniences to the subject and, also, the reasonably expected benefits [24-27]. Other elements included in the informed consent, according to the same source, refer to the alternative procedure(s) or treatment(s) that may be available to the subject, and their potential significant benefits and risks, the compensation and/or treatment available to the subject in the event of study-related harm, and the anticipated payment, if any, to the subject for participation in the study [24-27]. The list of all elements that constitute an informed consent form is too extensive to be reproduced here, but this complexity explains the long time necessary for the investigator to explain the totality of the relevant aspects to each participant in order to obtain his/her approval to participate in the trial.

Patient safety and monitoring of adverse events

Investigators are responsible for carefully monitoring the psychobiological parameters of each participant in a trial, ensuring that subjects are not exposed to avoidable health risks [24-27]. This process presumes a regular verification for the existence of adverse reactions, offering adequate interventions if these appear and discontinuing participants' involvement if they develop a serious adverse event. Failure to comply with this principle is a severe form of malpractice and a clear violation of the core principles of the Declaration of Helsinki [28-30].

For example, if an investigator continues to administer an investigational product to a patient despite clear signs suggesting the onset of severe side effects, he or she is engaging in a form of negligence that can have severe legal consequences far beyond the violations of ethical conduct. In this area are placed the cases when participants who remain pregnant during the clinical trials are still receiving the investigational product or when adverse events to the experimental drugs are treated with medications not allowed by the study protocol, thus disregarding the potential of pharmacologically dangerous interactions. According to a study [34] focused on the understanding of potential trial participants regarding the monitoring and communication of serious adverse events during a clinical trial, it was observed that their awareness of safeguards or regulations in this domain was very scarce; also, many of them expressed the desire to be more informed about the potentially serious adverse events and short reporting deadlines. The same study reported on the concerns of participants about potential financial conflicts of interest in monitoring and further reporting serious adverse events during a clinical trial [34].

In the same direction, the 2024 revision of the Declaration of Helsinki notes that unproven interventions focused on alleviating pain or suffering must not bypass ethical safety measures or avoid evaluation by controlled clinical trials [35], highlighting the importance of conducting an accurate assessment of all health parameters even in the most severe patients.

New tools have been suggested for the most accurate monitoring of safety in clinical trials, including those using graphical visualizations that are congruent with the FDA/EMA (European Medicines Agency) guidelines [36]. Such tools are interactive and support regular medical monitoring and oversight [36]. The National Institutes of Health in the US require data and safety monitoring boards for all phase III clinical trials, which are conceived as a supplementary barrier to errors in safety monitoring [37].

Data falsification and breaking the research integrity

The accuracy of data collection in the clinical research process and the integrity of the analysis of information regarding the efficacy and tolerability of the investigational product are essential to provide valid results. Ethical breaks and legal issues can be detected in this field when an investigator manipulates or falsifies clinical data to obtain some desired results [38,39]. Data falsification exerts

significant prejudice on the validity of research, endangers the patient's safety, and violates the core ethical principles of medicine.

For example, such an unethical approach can lead to the approval by competent institutions of harmful or ineffective treatments for clinical use, which can significantly endanger future patients [38-41]. Furthermore, new research could be based on a false presumption, and this could exponentially amplify the negative economic and medical consequences of a single false study [38-41].

Several examples of data falsification and research integrity break are: (a) selective reporting, which is a form of reporting only data that supports the drug's efficacy while omitting negative or inconclusive results; (b) data harvesting, a phenomenon that refers to the selective analysis of certain variables that fit a desired outcome, ignoring others; (c) partial monitoring of tolerability data, which may be observed when there is a lack of monitoring or inadequate reporting of adverse effects that occur during the study; (d) lack of adequate monitoring of participants after the study ends to confirm that the investigator ensures that any long-term effects of the drug are documented and managed appropriately; (e) underestimation of risks, which refers to the situation when the investigators minimize or ignore potential risks that expose participants to short, medium, and long-term negative effects [38-43].

Another example of phenomena that negatively interact with research integrity is the participation in clinical trials of investigators with insufficient experience or without enough credentials, and this is a direct violation of the Declaration of Helsinki [28-30]. Thus, allowing individuals without the necessary certifications or knowledge to conduct or supervise critical aspects of a trial is an example of ethical misconduct [28-30]. Failure to provide adequate training to staff on ethical practices, safety protocols, or specific clinical trial procedures is also a breach of research integrity [28-30].

Ethical integrity can also be breached by improper recruitment and enrollment of participants [28-30,38]. For example, the inclusion of ineligible participants might refer to the enrollment of individuals who do not meet the inclusion criteria for the study, such as those with contraindicated health conditions or who are already taking other medications prohibited by the study protocol. On the other hand, but in the same category of ethical breaches, the exclusion of eligible participants refers to discrimination against specific populations, such as vulnerable groups, in order to distort results or save time. Such examples are the inclusion of participants diagnosed with major depression and active suicide ideation, although the study protocol prohibits their enrollment, and, on the other hand, exclusion of patients with severe depression due to the investigator's fear they will be challenging to manage, although the study protocol allows their participation.

Ethical breaches may be derived from protocol deviations and protocol violations [44,45]. The first case refers to divergences between the study activities from the institutional review board (IRB)-approved protocol with minimal impact, while the second refers to divergences that reduce the quality or completeness of the data, inaccuracies in the informed consent form, or endanger the subject's safety, rights, or welfare [45]. For example, if the test procedures are modified or the treatment administration algorithm is changed during the trial without a clear rationale, these may affect the results and induce harmful reactions in the participants. Also, failure to adequately document protocol changes or deviations makes it impossible to assess their potential impact on the trial. Failure to report or address ethical concerns is a significant methodological and ethical or legal error that can be observed, for example, when an ethical review is neglected by failing to obtain approval from an IRB or ethics committee before the trial begins or failing to address ethical concerns raised during the review process [46].

Several ways to decrease the risk of protocol deviations are enhanced training for the investigators, regular monitoring visits, involvement of the Ethics committee in site monitoring, etc. [44]. In a study that explored 80 postgraduate dissertations, representing observational studies (74%) and interventional trials (10%), a significant proportion of protocol deviations (more than 42%) were due to nonreporting and incomplete documentation of the divergencies [47].

Consequences of malpractice in clinical trials

Clinical trial litigation has been rapidly escalating during the last decades, and defendants are not only principal investigators or sponsors but also IRBs, individual IRB members, study coordinators, etc. [48,49]. Beyond the legal repercussions, malpractice in clinical trials can have long-lasting effects on public opinion about medical research. Patients may become hesitant to participate in future clinical trials, fearing that their health may be at risk. As a consequence, the interest of the general public in research could decrease, and thus, the availability of new treatments for various disorders could be delayed, or potentially valuable drugs may even be abandoned.

Furthermore, the reputation of healthcare practitioners can be significantly damaged when cases of malpractice in clinical trials are discovered and exploited by mass media [50,51]. Such phenomena can fuel an environment of skepticism and mistrust, leading to the erosion of the relationship between the patient and the healthcare specialists. The impact is, consequently, negative not only at an individual level but also at a macro-social level, with consequences beyond the level of a research site or a certain clinical trial.

Examples of famous cases when ethical and legal violations of clinical research were detected

One of the first cases of ethical misconduct after the Nuremberg Trials, which brought to the general interest the dangers of experiments without ethical restraints, was related to the MKUltra studies (1955–1967) [52,53]. These involved „mind-control" techniques using LSD-25, and were sponsored by the CIA [52]. Many of the subjects were given LSD and other psychoactive substances without consent, and some were subjected to psychological manipulation; also, not all of the „investigators" were healthcare specialists, but they came from very diverse professional backgrounds, e.g., one of them was a magician, i.e., a student of Harry Houdini, while another was a CIA consultant with a shady history; tragically, this so-called experiment for mental illnesses became

medical torture not very unlikely to the Nuremberg Trials [52,53]. Different reports describe the effects of these experiments on mental health, including the Veterans Health Initiative Report in 2003 [53].

The study 329 (1994–2001) investigated the use of paroxetine and imipramine in adolescents, and this research was later found to have serious ethical and scientific flaws, including selective reporting of results [54,55]. An independent reanalysis of the data from Study 329 (the RIAT initiative) showed that acute and long-term paroxetine and imipramine were harmful and ineffective in adolescents with major depression [54]. In the original study, paroxetine proved itself well-tolerated and effective in that population on multiple outcomes, i.e., the Hamilton Depression Rating Scale (HAMD), Schedule for Affective Disorders and Schizophrenia for Adolescents-Lifetime version (K-SADS-L), and Clinical Global Impression (CGI), while the withdrawal rates due to adverse events were 9.7% vs. 6.9% (paroxetine vs. placebo) [55]. The RIAT analysis presented several ways in which the presentation of safety data in clinical trials may influence the apparent tolerability of a drug, e.g., the use of an idiosyncratic coding system, failure to transcribe all adverse events from clinical records to an adverse event database, or filtering data on adverse events through statistical techniques [55]. This case is interesting because it represents an argument to make it available for independent analysis of all primary data available from a clinical trial [56].

The Ranbaxy Case (2006-2008) involved a major Indian pharmaceutical company in a significant controversy related to drug safety, more specifically to the quality of various generic drug products, including gabapentin and the antibiotic ciprofloxacin [57]. Ranbaxy was accused of falsifying data in clinical trials, including trials of generic drugs, related to the purity, strength and quality of these generics, and the case resulted in the company being fined $500 million by the US Department of Justice for selling counterfeit drugs and submitting false data to the FDA [57]. Incomplete testing records and inadequate programs focused on the assessment of the stability characteristics of drugs were detected by an FDA inspection in the Paonta Sahib facility in 2006 [57].

Other doubts about the regulation authorities failing to keep up with ethical issues in clinical research in India have been raised [58]. Although most of the alleged ethical violations were not confirmed, the controversy about the clinical trials in India has decreased dramatically the trust in clinical research originated in India [58]. Lack of informed consent from volunteers, conflict of interests surrounding the members of independent ethics committees, suspicions about the use of vulnerable populations, and lack of insurance or compensation in case of serious adverse events were subjects presented by activists [58]. In 2017, a guideline passed by the Indian Council of Medical Research was launched to improve the quality of clinical research in that country [59]. These guidelines approach sensitive topics, like the procedure to obtain informed consent, the respect for voluntariness, the definition of vulnerable population, the assessment of the benefits vs. risks balance, and the compensation for harm derived from participation in clinical trials [59]. Also, regularization of the Ethical Committee structure and functions are included in these revised guidelines [59].

Prevention of malpractice in clinical trials

The complexity of clinical research has attracted numerous debates over the last decades, and national institutions with responsibilities in the field of drug regulation have initiated their own rules and norms, besides international or regional ones. EMA, WHO (World Health Organisation), and WMA are the leading institutions with expertise in the regularization of clinical research [60-65]. National agencies, like the FDA in the US or the PMDA (Pharmaceuticals and Medical Devices Agency) in Japan, are also regulatory organizations with rich experience and ethical guidelines dedicated to clinical research [66,67].

In order to decrease the risk of ethical misconduct and litigations in this field, such institutions with responsibilities in the domain of monitoring the research activity must provide continuing education and training to physicians involved in clinical trials, ensuring that they understand the ethical, legal, and scientific responsibilities they bear. The activity of pharmacovigilance is also a topic that needs to be regularized because this stage is essential for ensuring post-marketing feedback from the patients. Phase IV studies are not at all less important than other clinical trials due to their importance in maintaining clinical use of only those drugs that prove themselves useful and tolerable, even after they pass the pivotal trials. The real safety profile of a certain drug may be defined only by continuing surveillance, and this requires an intense effort from patients, doctors, and regulatory institutions [68].

There is a need for effective oversight mechanisms, including local ethics committees, which evaluate the ethical, methodological, and safety aspects of clinical trials before and during their implementation. These committees act as a core protection for human research participants due to their independent review of the ethical acceptability or proposal for human research [69]. The importance of these organisms has been mentioned in the previous chapter, as avoidance of the conflict of interest within IRBs/Ethical Committees was a topic raised in the controversy surrounding clinical research in India [59].

Also, the transparency of research data implies compliance with rigorous protocols, with clear documentation of all procedures, decisions and results, which can be audited at any time by competent national and international institutions. This aspect's importance was highlighted by the Study 329 case, where an independent re-analysis of the original data provided different results [54].

DISCUSSION

The progress recorded in the treatment of psychiatric disorders in the last six decades could not be possible without clinical research based on the dedication of the investigators and volunteers who contributed in a significant way to this endeavor. Like any scientific domain, clinical research is not free of ethical and legal challenges, especially because, due to its sensitive nature, it mixes epistemological aspects (i.e., the experimental nature of the investigational process), with axiological (i.e., the liberty of the individual as a core value), and ontological ones (e.g., the biological vs. spiritual causation of our mental life). Thus, hypersensitive topics are

related to each dimension; starting from the acknowledgment of the participants that they assume certain health risks in a clinical trial, continuing with the voluntariness vs. coercion dilemma when being recruited for a study, or with the liberty to decide when to withdraw from a trial, all these aspects may be negatively exploited and consequently may trigger ethical misconduct and litigation. Clinical research has received a lot of attention from both the scientific world and the public, not to mention the vehicle between the two, i.e., the media. Avoiding dogmatic thinking and understanding the complexity of clinical research is important for any investigator, as is the ability of scientists to maintain the transparency of the research to society, which is the final beneficiary of their work. The legislation in the field of clinical trials is an evolving organism, and the Declaration of Helsinki is the result of the conjugated effort of society and the scientists trying to prevent the repeating of tragic ethical misconduct as in the Nuremberg Trials, MK Ultra experiments, etc.

Because the number of clinical trials is continuously increasing as a result of the social pressure to find more performant and more tolerable pharmacological agents, not to mention the need to respond to newer threats to human health, there is an ever-higher need to control the potential risk factors for ethical deviations in clinical research. Therefore, the vulnerabilities related to the clinical research methodology explored in this review, i.e., those about the obtaining of informed consent, those connected to patients' safety, and those derived from data falsification, need to be continuously monitored and regulated by authorized institutions. The failure to do so would lead to a decrease of public trust in clinical research and virtually erase the line between scientific, validated-through-trials pharmacological agents and any other substance promoted by non-regularized commercial entities. This is a very important and actual topic because psychedelics (LSD included) or other substances with a risk of addiction are nowadays explored again for the use of various mental disorders, while various therapies with innovative mechanisms (e.g., focused on immune factors or gene modulation) are also emerging as potential solutions for multiple, psychiatric or somatic, illnesses [70-75]. Therefore, a continuous updating of ethical guidelines is needed to protect the participants in clinical trials from any type of abuse and to allow the investigators to work in a legally secure environment.

CONCLUSION

Pharmacological research activity is an essential component of the approach aimed at increasing the quality of medical practice by multiplying the existing therapeutic options for a specific medical condition. Evolution in the field of medicine is impossible to achieve, at least taking into consideration the current level of scientific knowledge, without clinical trials. Through this type of activity, progress in pharmacology is ensured, and the quality of patients' lives is increased while their chances of functional recovery and prognosis are improved.

Ethical and legal risks in clinical research derive mainly (but in no way exclusively) from (1) irregularities in obtaining informed consent of participants in the study, (2) failure of investigators to respect the safety of participants in the clinical study, and (3) incorrect reporting of data obtained from the research.

Controlling these risks involves respecting the stages of professional training of clinical trial investigators, as well as the efficient functioning of institutional control mechanisms in the field of pharmacological research.

Conflicts of interest and sources of funding

The authors declare no conflict of interest. No artificial intelligence automatically generated text was inserted in this manuscript, and no image was previously published in another journal or is under consideration of being published elsewhere. This research received no external funding.

Authors' contribution

Conceptualization, O.V, A.M.C.., and A.G.M.; methodology, B.M.P.; formal analysis, O.V, A.M.C.; investigation, O.V., A.M.C., B.P.M., A.G.M.; resources, O.V.; data curation, A.M.C..; writing—original draft preparation, O.V., A.M.C.; writing—review and editing, O.V., A.M.C., B.M.P.; visualization, A.G.M.; supervision, O.V., A.M.C.; project administration, O.V. All authors have read and agreed to the published version of the manuscript.

Ethics approval and consent to participate

Not applicable.

Patient consent for publication

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